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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/934,060 | 08/21/2001 | Anthony Louis Devico | 4115-144 CIP | 8085 |

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INTELLECTUAL PROPERTY / TECHNOLOGY LAW
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| EXAMINER | |
|---|---|
| WINKLER, ULRIKE | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1648 | 17 |

DATE MAILED: 11/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/934,060 | DEVICO ET AL. | |
| | Examiner | Art Unit | |
| | Ulrike Winkler | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *08 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-57* is/are pending in the application.

4a) Of the above claim(s) *17-54,56 and 57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 5-16* is/are rejected.

7)☒ Claim(s) *2-4 and 55* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6,8,10,12* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

Applicant's election with traverse of Group I (claims 1-16) with the further lection of Group C (SEQ ID NO 4, comprising a viral coat protein SEQ ID NO:30 – spacer – a viral receptor SEQ ID NO:26) in Paper No. 16 is acknowledged. The traversal is on the ground(s) that the product and method claims are not patenably distinct because the method claims utilize the instantly claimed polypeptide. This is not found persuasive because the method of inhibiting viral replication can be achieved using a materially different compound to inhibit viral nucleic acid replication (such as AZT).

The requirement is still deemed proper and is therefore made FINAL.

Applicants have requested rejoinder according to MPEP 8.321.04. A rejoinder of claims is possible at later date if the product is eventually found patentable, the claims directed to the process of making or using the patentable product, previously withdrawn from consideration as a result of a restriction requirement, may be subject to being rejoined. In the event of rejoinder, the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. If the application containing the rejoined claims is not in condition for allowance, the subsequent Office action may be made final, or, if the application was already under final rejection, the next Office action may be an advisory action.

### *Sequence listing*

Applicant's CRF and paper sequence listing have been entered.

***Information Disclosure Statement***

An initialed and dated copy of Applicant's IDS form 1449, Paper No. 6 (September 24, 2001) and Paper No. 6 (October 3, 2001) [note 2 entries for Paper No.6], Paper No. 8 (June 16, 2002), Paper No. 10 (October 29, 2002) and Paper No. 12 (February 19, 2003), are attached to the instant Office Action.

***Drawings***

The drawings have been approved by the Draftsperson.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 8 and 11 are rejected under 35 U.S.C. 102(e) as being anticipated by Young et al. (U.S. Pat. No. 6,060,316).

The instant invention is directed to a chimeric polypeptide comprising a viral coat polypeptide from a retrovirus and a viral receptor. The sequences are linked by an amino acid spacer allowing the receptor and ligand to bind each other.

Young et al. discloses the production of soluble viral receptor and ligand fusion moieties of the soluble viral receptor-ligand fusion molecule can be directly bonded together or through a linking moiety. Where one or both of the moieties are polypeptides, a peptide bond or peptide

linker is preferred, thereby obtaining a "fusion protein" of the two moieties which can be expressed by a single nucleic acid construct in series. The two moieties can alternatively be linked directly or indirectly other than via a peptide bond or peptide linker, thereby obtaining a "conjugate" (see column 9, lines 40-50). If a linking moiety is employed to link the two moieties. The linker can preferably be a flexible linker and sufficient in length to separate the moieties in space, thereby not restricting the ability of the soluble viral receptor-ligand fusion molecule to bind independently and maintain the proper conformation. Where both moieties are polypeptides, the linker moiety will generally be a peptide, polypeptide, or a "pseudopeptide" (see column 9 line 66 to column 10 line 5). The reference indicates that the viral surface protein (envelope) is generally the viral protein that binds the cell and activated viral entry (see column 8, lines 48-52), and the cellular receptor for retroviruses is CD4 (see column 8, lines 58-61). Therefore, the instant invention is anticipated by Young et al.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 5-16 rejected under 35 U.S.C. 103(a) as being unpatentable over Young et al (U.S. Pat. No. 6,060,316) and DeVico et al. (U.S. Pat. No. 5,843,454, IDS) or DeVico et al. (U.S. Pat. No. 5,518,723, IDS) in view of Stratagene Catalog (1997/1998).

The instant invention is directed to a chimeric polypeptide comprising a viral coat polypeptide from a retrovirus and a viral receptor. The sequences are linked by an amino acid spacer allowing the receptor and ligand to bind each other. The chimeric polypeptide can comprise a tag.

Young et al. teach the production of a soluble viral receptor and ligand fusion moieties which can be directly bonded together or through a linking moiety. Where one or both of the moieties are polypeptides, a peptide bond or peptide linker is preferred, thereby obtaining a "fusion protein" of the two moieties which can be expressed by a single nucleic acid construct in series. The two moieties can alternatively be linked directly or indirectly other than via a peptide bond or peptide linker, thereby obtaining a "conjugate" (see column 9, lines 40-50). If a linking moiety is employed to link the two moieties. The linker can preferably be a flexible linker and sufficient in length to separate the moieties in space, thereby not restricting the ability of the soluble viral receptor-ligand fusion molecule to bind independently and maintain the proper conformation. Where both moieties are polypeptides, the linker moiety will generally be a peptide, polypeptide, or a "pseudopeptide" (see column 9 line 66 to column 10 line 5). The

reference indicates that the viral surface protein (envelope) is generally the viral protein that binds the cell and activated viral entry (see column 8, lines 48-52), and the cellular receptor for retroviruses is CD4 (see column 8, lines 58-61). The reference does not teach using the composition in a pharmaceutically acceptable carrier.

DeVico et al. disclose in both patents a CD4-gp120 complex that has been covalently linked using a reactive spacer molecule. The reference teaches using the complex as a vaccine. The reference teaches that the interaction between the virus coat protein and the virus receptor exposes cryptic epitopes that are not present with the viral coat protein or the CD4 receptor alone (see table 1). Gp120 and CD4 have an affinity for one another and spontaneously form a complex when placed in a solution together. The reference does not teach using an amino acid spacer in the production of the antigenic complex.

Stratagene Catalog discloses the use of protein expression vectors using an affinity tag for the purpose of easily purifying the desired protein. The reference does not disclose the expression of a virus coat/virus receptor fusion protein.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize a chimera for the production of the gp120-CD4 complex. The chimera as taught by Young et al. requires the single process step utilizing affinity purification after the expression of the fusion protein. One having ordinary skill in the art would have been motivated to make a gp120-CD4 chimera to achieve the conformational complex as taught by DeVico et al. which would have the advantage of requiring less process steps in order to achieve the same function. The prior art requires purifying the CD4 and the gp120 proteins separately allowing them to interact and then chemically cross linking followed by the removal of the excess cross

linker. One having ordinary skill in the art would have a high expectation of success when expressing the complex as a single polypeptide. The addition of amino acid linkers would have been obvious to the ordinary artisan in order to alleviate potential folding constraints in the fusion protein as suggested by Young et al. (see column 10, lines 1-5). The use of an expression or affinity tag for the purpose is well established in the art as shown by the availability of such tools using commercial vendors (Stratagene Catalog). If the addition of the affinity tag produces an unexpected result, applicant will need to point out what the unexpected result are. Therefore, the instant invention is obvious over Young et al. and DeVico et al. in view of Stratagene Catalog.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 5-11 and 15, 16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 3 of U.S. Patent No. 5,518,723 in view of Young et al (U.S. Pat. No. 6,060,316).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant invention is directed to a chimeric polypeptide comprising a viral coat polypeptide sequence and a viral receptor. The sequences are linked by an amino acid chain that function to allow formation of an interacting complex between the virus coat polypeptide sequence and receptor polypeptide sequence (specification, page 14, line 23-31). The U.S. Patent No. 5,518,723 discloses CD4-gp120 (claim 1) which is drawn to an immunogenic complex comprising gp120 covalently bonded to CD4 so that cryptic epitopes are exposed. The patent includes the complex in a pharmaceutically acceptable carrier. A peptide bond is a covalent bond because it involves the sharing of electrons. Young et al. teach the production of a chimera between a viral coat protein (Env) and cell surface receptor (CD4) for the production of a fusion protein complex.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize a chimera for the production of the gp120-CD4 complex as taught by DeVico et al. The gp120 and CD4 molecules have a natural affinity for another and form the complex spontaneously. One ordinary skill in the art would have been motivated to make a gp120-CD4 chimera to reduce the process steps in order to achieve the same function. The chimera as taught by Young et al. requires the single process step. One having ordinary skill in the art would have a high expectation of success when expressing the complex as a single polypeptide. The addition of amino acid linkers would have been obvious to the ordinary artisan in order to alleviate potential folding constraints in the chimera as suggested by Young et al.

Claims 1, 5-11 and 15, 16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 5,843,454 in view of Young et al. (U.S. Pat. No. 6,06,316).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant invention is directed to a chimeric polypeptide comprising a viral coat polypeptide sequence and a viral receptor. The sequences are linked by an amino acid chain that function to allow formation of an interacting complex between the virus coat polypeptide sequence and receptor polypeptide sequence (specification, page 14, line 23-31). The U.S. Patent No. 5,843,454 discloses CD4-gp120 (claim 1) is drawn to an immunogenic complex comprising gp120 covalently bonded to CD4. The patent includes the complex in a pharmaceutically acceptable carrier. A peptide bond is a covalent bond because it involves the sharing of electrons. Young et al. teach the production of a chimera between a viral coat protein (Env) and cell surface receptors (CD4) for the production of a complex.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize a chimera for the production of the gp120-CD4 complex as taught by DeVico et al. The gp120 and CD4 molecules have a natural affinity for another and form the complex spontaneously. One ordinary skill in the art would have been motivated to make a gp120-CD4 chimera to reduce the process steps in order to achieve the same function. The chimera as taught by Young et al. requires the single process step. One having ordinary skill in the art would have a high expectation of success when expressing the complex as a single polypeptide. The addition of amino acid linkers would have been obvious to the ordinary artisan in order to alleviate potential folding constraints in the chimera as suggested by Young et al.

### *Claim Objections*

Claims 2-4 and 55 are objected to because of the following informalities: The claims are dependent on a rejected claim. Appropriate correction is required.

### *Conclusion*

Claims 2-4 and 55 are objected to.

Claims 1, 5-16 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 703-308-8294. The examiner can normally be reached M-F, 8:30 am - 5 pm. The examiner can also be reached via email [ulrike.winkler@uspto.gov].

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 703-308-4027.

The official fax phone number for the organization where this application or proceeding is assigned is 703-872-9306; for informal communications please use 703-746-3162.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

ULRIKE WINKLER, PHD.
PATENT EXAMINER 11/13/03